REMARKS

Upon entry of the foregoing amendment, claim 1 has been amended to correct a matter of form. The substance of claim 32 has been incorporated into claim 31, and claim 32 has thus been canceled as being redundant. Claims 6-30, 32 and 36-38 have been canceled without prejudice. Claims 1-5, 31 and 33-35 remain pending. No new matter is introduced by the amendment.

Entry of the foregoing amendment is respectfully requested. Applicants submit that the amendment overcomes substantial issues relating to the patentability of the claims and places the application in condition for allowance, as discussed in more detail below. Additionally, the amendment also cancels non-elected subject matter (claims 9-30). As all the remaining issues have been overcome by amendment, Applicants submit that entry thereof would serve to expedite prosecution and reduce the burden of prosecution on the Patent Office.

Applicants respectfully request reconsideration of the rejections made in the September 8, 2004 office action (Office Action).

The Utility Rejection Under 35 USC § 101 Should Be Withdrawn

Upon entry of the foregoing amendment, claims 1-5, 31 and 33-35 stand rejected under 35 U.S.C. § 101 for alleged lack of utility, the rejection of claims 6-8, 32 and 36-38 having been rendered moot by cancellation of those claims. Applicants submit that claims 1-5, 31 and 33-35 are in compliance with the requirements of 35 U.S.C. § 101; thus this ground of rejection should be withdrawn.

Applicants submit that the claimed compounds possess a specific utility that is both credible and substantial within the meaning of § 101. The Office Action affirms that the utility of the claimed nucleic acids is credible, but incongruously avers that the credible utility is neither substantial nor specific. Applicants gratefully acknowledge the Office Action's holding that the asserted utility is credible, and submit that the credible utility is also substantial and specific.

The Office Action takes issue with the substantiality and specificity of the utility of the invention. It is noted that the claimed compound is a nucleic acid that codes for CLAN-A, which the specification indicates is capable of activating pro-caspase-1. (Specification page 16, lines 24-27). Thus, the utility of the claimed nucleic acids do indeed hinge on the utility of the encoded protein. However, Applicants take issue with the conclusion stated in the Office Action that CLAN-A has no specific and substantial utility.

Applicants note that the utility guidelines do not require that a gene have a medicinal or therapeutic utility. According to the utility guidelines, the requirement that the invention possess a specific and substantial utility "excludes 'throw-away,' 'insubstantial,' or 'nonspecific' utilities, such as the use of a complex invention as landfill as a way of satisfying the utility requirement. . . ." (66 Fed. Reg. 1092, 1096 (2001)). The specification clearly states that CLAN-A activates the pro-caspase-1 to form caspase-1. (Specification, page 16, lines 24-27). The specification also clearly states caspase-1 is involved in inflammation and apoptosis. (Specification, pages 3, 7, 16). These biological activities are not "throw away" activities in the vein of using CLAN-A as landfill. (66 Fed. Reg. 1092, 1096). Rather they are complex biological activities of importance in

various biological processes such as apoptosis and inflammation. (Specification, pages 3, 5, 16).

Applicants maintain that the Office Action's reliance on *Brenner v. Manson* 383 U.S. 519, 148 USPQ 689 (1966) is misplaced. While the *Manson* Court did articulate a necessity that the invention possess a specific utility, the facts of the *Manson* case do not square with those of the instant invention. In *Manson*, the inventor claimed a process of making steroids, asserting that the process possessed utility simply because it was capable of making a class of compounds for which no specific utility was stated in the specification. In contrast, the instant specification asserts a specific biological activity for CLAN-A -- activation of procaspase-1 to form caspase-1, which is well-known to be involved in apoptosis and inflammation. (Specification, page 16). So it is not correct to state, as the Office Action does, that the "cited utilities of pro-caspase-1 activation or inhibition have less 'real world' significance than the amount of utility found insufficient by the Supreme Court in *Brenner v. Manson*," as the *Manson* application stated no utility whatsoever, whereas the present specification recites the very specific utility of activation of pro-caspase-1.

Nor is the gene encoding CLAN-A, as the Office Action states, an orphan gene. One skilled in the art would recognize the term "orphan gene" to indicate that the nucleic acid had been identified as a gene because it possessed the hallmarks of a gene (such as a promoter, start codon, stop codon, etc.), but failed to possess a known activity. In contrast, SEQ ID NO:96 encodes a polypeptide of SEQ ID NO:97, which itself possesses pro-caspase-1 activation activity. It goes against all logic to label a gene "orphan" when that

gene has been identified as possessing the ability to interact with and affect the activity of a known and important biological compound, pro-caspase-1.

Applicants further take issue with the Office Action's reliance on its observation that the specification teaches that "Clan [sic, CLAN] molecules can have opposing functions, so that some Clan [sic, CLAN] molecules may trigger pro-caspase-1 activation while others may inhibit this activation." (Office Action, page 3). This observation is irrelevant in light of Applicants' specific teaching that CLAN-A, the only CLAN that is relevant to the instant claims, activates pro-caspase-1. The Office has already restricted the various CLANs from one another, and so has admitted that they have separate, patentably distinct properties. The use of a general statement relating to the genus of CLANs against CLAN-A is thus illogical and should be withdrawn.

Applicants further traverse the statement in the Office Action that "Applicant's [sic, Applicants'] own paper supports a conclusion that there is no 'real world' use, other than further investigation, for SEQ ID NO:97." This is not a fair assessment of the teaching of the cited Damiano et al. reference. The Daminano et al. reference is in agreement with the instant specification as to the activity of CLAN-A as an inducer of pro-caspase-1 activation by the induced proximity effect. (Damiano et al. at 82, column 1). The Damiano et al. reference also corroborates the connection between CLAN-A pro-caspase-1 activation and inflammation. (Id.) These teachings do not contradict the clear teaching of the instant application regarding the biological activity of CLAN-A. That there are other potential utilities remaining to be elucidated for CLAN-A is immaterial, as only one utility need be apparent for the invention to be patentable.

For the reasons stated above, Applicants submit that the rejection under 35 U.S.C. § 101 is untenable and should be withdrawn.

The Pending Claims are Enabled Under 35 U.S.C. § 112, First Paragraph

Upon entry of the foregoing amendment, claims 1-5, 31 and 33-35 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement, the rejection of claims 6-8, 32 and 36-38 having been rendered moot by cancellation of those claims. Applicants submit that claims 1-5, 31 and 33-35 are in compliance with the requirements of 35 U.S.C. § 112, first paragraph; thus, this ground of rejection should be withdrawn.

Applicants first take issue with the Office Action's characterization of claims 1-8 as being drawn to a "system and method of screening using SEQ ID NO:97." This is incorrect. Claim 1 is clearly drawn to: "An isolated nucleic acid molecule encoding a CARD-containing polypeptide, which is: DNA encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 97." Hence, as regards claim 1, Applicants need only teach how to make and use the claimed nucleic acid. As the sequence of SEQ ID NO:97 is disclosed in the specification, as are the codons that code for such amino acid sequence (see for example SEQ ID NO:96), Applicants have clearly taught one of skill in the art how to make the claimed invention. Applicants submit that the question of enablement should be re-evaluated, taking into account the actual scope of the claimed subject matter.

In any case, the only remaining controversy appears to be whether Applicants have taught how to use the claimed sequence. While the Office Action scrupulously sets forth an *In re Wands*-style analysis, it is clear that this arm of the rejection under § 112, first

paragraph, is mostly co-extensive with the utility rejection above. To the extent, then, that the § 112, first paragraph, rejection is premised on an alleged lack of utility, Applicants incorporate here their arguments above in their entirety. To the extent that the rejection relies on the aforementioned *Wands* analysis, Applicants offer the following remarks.

As stated above, claim 1 is limited to a nucleic acid encoding SEQ ID NO:97. The subordinate claims further limit the nucleic acid to a specific sequence (SEQ ID NO:96, claim 2), cDNA, vectors and recombinant cells containing that nucleic acid sequence (claims 3-5, respectively) and a nucleic acid that hybridizes to SEQ ID NO:96, as well as probes, etc. comprising SEQ ID NO:96 (claims 31 and 33-35). The specification teaches how to make SEQ ID NO:96 and use it to make vectors, probes, etc.

Regarding the breadth of the claims, Applicants submit that the pending claims do not encompass oligonucleotides as short as 15 contiguous bases. Rather, all the pending claims require that the nucleic acid code for full-length SEQ ID NO:97. This is fully supported by the instant disclosure. Accordingly, this premise for the enablement rejection is untenable and should be withdrawn.

Regarding the amount of guidance in the specification, it is not true that there are not particular uses specified for SEQ ID NO:97. As discussed in detail above, the utility of SEQ ID NO:97 is clearly set forth in the specification; and Applicants' remarks in regard to the utility requirement, above, are incorporated here by reference.

As regards the lack of working examples, Applicants submit that it is unnecessary that the specification provide a working example of how to detect or diagnose a specific disease using CLAN-A. The specification clearly indicates that CLAN-A activates pro-

caspase-1 cleavage and activation, thereby implicating its use in diagnosis and treatment of caspase-1 linked diseases such as those set forth on pages 86-87 of the specification. Applicants submit that, given that there has been no competent showing that would contradict the asserted utility, and given the extensive teaching of the specification, no working examples are necessary to use the claimed compounds as probes and diagnostic agents, for example.

As regards the amount of guidance in the prior art, Applicants submit that the Office Action's reliance Damiano et al. is adequately rebutted above. Thus, those comments are incorporated here by reference.

Applicants submit that the level of skill in the art is indeed high, and that the person of skill in the art would have found it routinely within that skill to make a compound encoding SEQ ID NO:97 (such as SEQ ID NO:96), to make CLAN-A using that compound (such as by incorporating it into a vector and then into a recombinant cell to manufacture CLAN-A). Likewise the person skilled in the art would know how to use the compound encoding SEQ ID NO:97 as a probe, as described in the specification, to detect CLAN-A expression in various tissues. As stated in the specification, the person skilled in the art would thus be able to detect aberrant expression of CLAN-A in a variety of tissues. (See specification, pages 86-88). Given the link between caspase-1 activity and inflammation and apoptosis, the person of skill in the art would likewise have been more than capable of using the nucleic acid as a probe as described in the specification.

Regarding the predictability of the art, Applicants submit that the Office Action's reliance on Dujon, 12(7), 263-270 (1996) is completely out of place. As discussed in

detail above, the CLAN gene does not even remotely satisfy the art-accepted definition of an orphan gene. SEQ ID NO:96 encodes CLAN-A, which possesses specific activity as a pro-caspase-1 activator. Thus, whatever one may glean from Dujon regarding the predictability of the art for orphan genes does not even remotely relate to the present invention.

As regards the quantity of experimentation required to practice the claimed invention, the Office Action makes no more than a conclusory statement that the amount of experimentation would be "extremely large." Applicants submit that this conclusion appears to be premised on the incorrect identification of the CLAN gene as being an "orphan gene." However, Applicants point out that they have already clearly identified the nexus between CLAN-A and a known biological compound pro-caspase-1, whose biological import is discussed in detail above and remains unrebutted. Thus, the person skilled in the art would have all the knowledge necessary to employ the CLAN-A polynucleotide for making CLAN-A, which has been shown to have utility as a pro-caspase-1 activator. Applicants therefore submit that the amount of experimentation necessary to practice the invention would not be excessive for the person skilled in the art.

Applicants have rebutted all of the points raised in the Office Action in support of the enablement rejection. Applicants thus submit that the Office Action fails to present a tenable *prima facie* case of non-enablement. Therefore the rejection under § 112, first paragraph, should be withdrawn.

The Amended Claims Comply With The § 112, First Paragraph Description Requirement

Upon entry of the amendment, s claims 31 and 33-35 stand rejected as lacking written description, the rejection of claims 36-38 having been mooted by their cancellation, without prejudice, above. Applicants note that the foregoing amendment introduces the limitation of canceled claim 32 into claim 31. As canceled claim 32 was not subject to this ground of rejection, and as remaining claims 36-38 depend from claim 31, it is submitted that this ground of rejection has been overcome and should be withdrawn.

The Rejection Under § 102(b) Over Adams et al. Should Be Withdrawn

Upon entry of the amendment, claims 31 and 33-35 stand rejected under 35 USC § 102(b) as being anticipated by Adams et al., claim 6 having been canceled, without prejudice, above. Applicants respectfully traverse this rejection. Applicants note that claim 32, the entirety of which has been incorporated into claim 31, was not subject to this rejection. Accordingly, claim 31 should not be subject to this rejection either. By extension, claims 33-35, which depend ultimately from claim 31, should also not be subject to this rejection. Therefore, withdrawal of the rejection is respectfully requested.

Conclusion

Applicants submit that the foregoing amendments and remarks represent a *bona fide* response to the outstanding Office Action and that the pending claims are in condition for allowance. Such action is therefore requested.

If the Primary Examiner finds that allowance may be expedited, Applicants invite him to contact the undersigned directly at the telephone number below.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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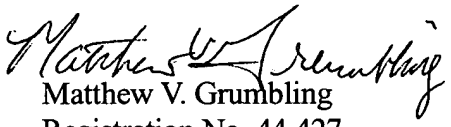

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